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Outcomes of single organism peritonitis in peritoneal dialysis: Gram negatives versus gram positives in the Network 9 Peritonitis Study

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Outcomes of single organism peritonitis in peritoneal dialysis: Gram negatives versus gram positives in the Network 9 Peritonitis Study. The use of the "peritonitis rate" in the management of patients undergoing peritoneal dialysis is assuming importance in comparing the prowess of facilities, care givers and new innovations. For this to be a meaningful outcome measure, the type of infection (causative pathogen) must have less clinical significance than the number of infections during a time interval. The natural history of *Staphylococcus aureus*, pseudomonas, and fungal peritonitis would not support that the outcome of an episode of peritonitis is independent of the causative pathogen. Could this concern be extended to other more frequently occurring pathogens? To address this, the Network 9 Peritonitis Study identified 530 episodes of single organism peritonitis caused by a gram positive organism and 136 episodes caused by a single non-pseudomonal gram negative (NPGN) pathogen. Coincidental soft tissue infections (exit site or tunnel) occurred equally in both groups. Outcomes of peritonitis were analyzed by organism classification and by presence or absence of a soft tissue infection. NPGN peritonitis was associated with significantly more frequent catheter loss, hospitalization, and technique failure and was less likely to resolve regardless of the presence or absence of a soft tissue infection. Hospitalization and death tended to occur more frequently with enterococcal peritonitis than with other gram positive peritonitis. The outcomes in the NPGN peritonitis group were significantly worse (resolution, catheter loss, hospitalization, technique failure) compared to coagulase negative staphylococcal or *S. aureus* peritonitis, regardless of the presence or absence of a coincidental soft tissue infection. Furthermore, for the first time, the poor outcomes of gram negative peritonitis are shown to be independent of pseudomonas or polymicrobial involvement or soft tissue infections. The gram negative organism appears to be the important factor. In addition, the outcome of peritonitis caused by *S. aureus* is worse than that of other staphylococci. Thus, it is clear that all peritonitis episodes cannot be considered equivalent in terms of outcome. The concept of peritonitis rate is only meaningful when specific organisms are considered.

Infectious complications are the major cause of morbidity and technique failure in a peritoneal dialysis program [1–3]. Peritonitis rates are being utilized as an outcome measure, in particular for comparing facilities or technical innovations. For "peritonitis rate" to be a meaningful measure, it is presumed that each episode of peritonitis will have reasonably equivalent short- and long-term outcomes. This premise does not appear to be valid. Peritonitis caused by certain pathogens such as pseudomonads (xanthomonads) and fungi is associated with increased catheter loss and transfer to hemodialysis [4–8], while peritonitis due to *Staphylococcus epidermidis* has a higher resolution rate than peritonitis caused by other pathogens [9–11]. Polymicrobial peritonitis is thought to originate from a bowel leak [12–14]. Thus, one would expect a worse outcome from a bowel leak etiology rather than from an infection caused by touch contamination. The source of gram negative organisms in peritoneal dialysis associated peritonitis has been speculated to be either a gastrointestinal or skin source [5, 11, 14]. Pseudomonas and polymicobes can bias an outcomes analysis of gram negative peritonitis. For example, it is uncertain if the outcomes of peritonitis caused by a single non-pseudomonal gram negative (NPGN) organism are clearly different than those caused by various gram positive organisms.

The Tri-State Renal (Network 9) of the Health Care Finance Administration End-Stage Renal Disease Networks performed a year long prospective study of all peritonitis episodes. Of interest are the differences between infections with single gram negative or gram positive organisms and among *S. aureus* and other staphylococci. We hypothesized that: (1) there is a difference in outcomes between NPGN peritonitis and gram positive peritonitis; (2) there is a difference in demographics between patients experiencing their first episode of peritonitis with a gram negative versus a gram positive organism; (3) there are outcome differences between gram negative and gram positive episodes independent of pseudomonal or polymicrobial involvement or soft tissue infections (STI, exit site and catheter tunnel tract); (4) there are outcome differences among *S. aureus* peritonitis, other staphylococci and other gram positive organisms; (5) the outcome difference among *S. aureus* peritonitis and other staphylococci is independent of STIs.

METHODS

Network 9 (Indiana, Ohio, Kentucky, ESRD Tri-State Renal Network, HCFA contract #500-91-0014) prospectively evaluated all 1930 patients undergoing peritoneal dialysis (PD) at the 68

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centers in this Network for one year starting on 1/1/91. For each PD patient in their unit every dialysis facility completed a detailed patient identification questionnaire which included demographic data. An additional "event" questionnaire form was completed for each peritonitis episode. This included information about signs, symptoms, organisms cultured, treatment, and outcome. The event forms were sent to the Network 9 office in Indianapolis where the data were entered into the computerized data base.

The nature of the data collected as well as data validation was performed by several techniques and described in detail elsewhere [4, 9]. Dialysis facilities had incentives to participate accurately in the study, in particular because they would receive facility specific information for their quality assurance programs. Validation included analyses of reported cases versus those expected based on known established Network 9 rates during the first months of the study. Discrepancies were identified and these facilities were telephoned and visited as necessary to insure compliance with reporting. The total number of estimated missed peritonitis episodes represents from 6% to 8% of the total number of reported peritonitis episodes.

The Network 9 Peritonitis and Catheter Survival Study defined resolution of peritonitis as the clearing of peritoneal dialysate effluent on visual inspection after antibiotic therapy. The printed study instructions specifically mandated that "a separate infection event is defined as peritonitis due to a different organism or an infection from the same organism after a 14 day infection-free interval without antibiotics." All cases presented in this communication fit this definition. By this definition reinfections would be included in this analysis, except for the demographic comparison, which were first episodes only (see below). Further definitions (such as soft tissue infection, bowel perforation) were left to the facilities. Non-resolution was arbitrarily defined as the lack of clearing after up to three courses of antibiotic therapy. A course of antibiotics was defined as the addition of any new (different) antibiotic or different combination of antibiotics, without a specific duration of therapy. If the peritonitis did not resolve with three courses of antibiotics, it was classified as non-resolution. The additional outcome parameters catheter removal, transfer to hemodialysis, and death were captured on the event forms totally independent of resolution of peritonitis with antibiotic therapy. Thus, it was possible for a peritonitis episode to be reported that had not "resolved," but in which the catheter had not been removed or the patient had not been transferred to hemodialysis or had not died. There were 59 such episodes in the gram positive group (11.1%) and 17 episodes in the NPGN group (12.5%). These episodes were included in the catheter not removed, no transfer to hemodialysis, and no death groups during outcome analysis. The outcomes catheter removal, resolution, transfer to hemodialysis (HD), and death were not mutually exclusive so that a patient could have resolved his/her infection and have transferred to hemodialysis. A soft tissue infection (STI) is an exit site or catheter tunnel tract infection defined by the individual facilities. As detected in the questionnaire, a STI was a coincidental infection to the peritonitis event and did not have to be caused by the same organism as that causing peritonitis, nor was the pathogen from the STI necessarily recorded. The STI was merely present or absent on the event form.

This analysis was confined to patients 20 years of age or older on 1/1/91 with a positive peritoneal effluent culture with a single pathogen isolated as either a gram positive or a NPGN organism.

Table 1. Organisms cultured from peritoneal dialysate

Gram positive	*N*	NPGN[a]	*N*
1) *Staphylococcus aureus*	149	1) *E. coli*	19
2) *Staphylococcus epidermis*[b]	220	2) Klebsiella	21
3) Other Staphylococci[b]	22	3) Enterobacter	19
4) Enterococcus	27	4) Serratia	9
5) Other gram positive	112	5) Acinetobacter	10
Total	530	6) Proteus	5
		7) Other NPGN's	53
		Total	136

[a] Non-pseudomonal gram negative

[b] In later tables these organisms are lumped as coagulase negative staphylococci (CNS).

Episodes of culture negative peritonitis were excluded due to the uncertainty of the cause and the Network 9 experience with culture negative peritonitis has been described in detail elsewhere [15]. If patients experienced an episode of gram positive peritonitis early in the year followed later in the year by NPGN peritonitis, it would result in the counting of the patient in each group. If the patient had two episodes of gram positive or NPGN peritonitis in a year (including reinfections), each episode represented a case. Ninety-five patients had two episodes and 39 patients had three or more episodes of peritonitis described in this report. Relapses were addressed in the 14 day instructions described above and were not counted as separate episodes. An additional demographic analysis was performed on patients with only their first clinical diagnosis of peritonitis occurring during the 1991 study period. This was done to remove the possible confounding effect of previous episodes of peritonitis [9]. An analysis of antibiotic therapy was complicated by the absence of a uniform treatment protocol. Therefore, we herein report only the length and route of therapy. The initial antibiotics utilized and outcomes related to specific antibiotics were the subject of a previous report [16]. Episodes of pseudomonal peritonitis are described elsewhere [4] and reiterated in the discussion below. The method of culture of peritoneal fluid and the antibiotic regimens used were determined by each facility. Statistical analysis was performed by chi square using SPSS, Fischer's exact test when cell size was small, and the *t*-test. Statistical significance was defined as a P value < 0.05. Data are described with a mean $\pm$ one SD.

RESULTS

There were 530 episodes of peritonitis caused by a single gram positive organism and 136 episodes of peritonitis caused by a single NPGN organism. One hundred thirty-four patients experienced 322 of the episodes and 344 patients experienced only one episode of peritonitis during 1991. The various organisms responsible are shown in Table 1. *S. aureus* and *S. epidermidis* were the etiologic agent in 69.6% of the episodes of gram positive peritonitis. During 1991, enterococcus comprised only 5.1% of the episodes of single organism gram positive peritonitis. *E. coli*, klebsiella, and enterobacter accounted for 43.4% of the single NPGN peritonitis episodes. Fever ($P < 0.01$), nausea/vomiting ($P < 0.02$), and abdominal pain ($P < 0.04$) occurred more frequently in NPGN and *S. aureus* peritonitis than in peritonitis caused by coagulase negative staphylococci. There was a suggestion of an increased incidence of bowel perforation in the NPGN

Table 2. Outcomes

	CNS[a] N = 242	*S. aureus* N = 149	NPGN[b] N = 136	P value CNS-NPGN	P value *S. aureus*-NPGN
Resolved	83.8%	75.8%	58.8%	0.01	0.03
Catheter removed	4.6%	18.1%	30.0%	0.001	0.02
Hospitalization	17.9%	29.5%	44.1%	0.001	0.02
Transfer to HD	1.3%	8.7%	14.0%	0.001	0.2
Death	0.8%	3.4%	3.7%	0.1	1.0

[a] Coagulase negative staphylococci
[b] Non-pseudomonal gram negatives

Table 3. Outcomes in absence of exit site or tunnel infection

	CNS[a] N = 230	*S. aureus* N = 104	NPGN[b] N = 114	*P* value CNS-NPGN	*P* value *S. aureus*-NPGN
Resolved	84.6%	82.7%	63.2%	0.001	0.002
Catheter removed	3.1%	12.5%	23.7%	0.001	0.04
Hospitalization	17.5%	30.1%	43.0%	0.001	0.05
Transfer to HD	0.8%	2.9%	9.6%	0.002	0.06

[a] Coagulase negative staphylococci
[b] Non-pseudomonal gram negatives

Table 4. Outcomes in presence of exit site or tunnel infection

	CNS[a] N = 12	*S. aureus* N = 45	NPGN[b] N = 22	*P* value CNS-NPGN	*P* value *S. aureus*-NPGN
Resolved	66.7%	60%	36.4%	0.15	0.12
Catheter removed	33.3%	31.1%	63.7%	0.15	0.02
Hospitalization	25%	26.7%	50.0%	0.27	0.10
Transfer to HD	8.3%	22.2%	36.4%	0.11	0.25

[a] Coagulase negative staphylococci
[b] Non-pseudomonal gram negatives

Table 5. Demographics of patients with their first episode of peritonitis

	All gram positive N = 106	NPGN[a] N = 32	*P* value
Age ≥ 60	38.7%	39.1%	NS
Male	50.0%	50.0%	NS
Diabetes	41.5%	28.1%	NS
Afro-American	18.8%	25.8%	NS
≥2 infect in 1991[b]	33.0%	15.6%	0.075
Steroids[c]	23.9%	13.6%	NS

[a] Non-pseudomonal gram negatives
[b] Greater than or equal to 2 episodes of peritonitis in 1991
[c] Currently receiving steroids or have received them in the past

group compared to the gram positive group (NPGN = 3/136, vs. gram positive = 2/530, $P = 0.06$).

The outcomes for the episodes of staphylococcal and NPGN peritonitis are shown in Table 2. The outcomes are worst for NPGN, intermediate for *S. aureus* and best for CNS in all categories listed.

There was no difference in the incidence of STIs coincident with the episode of peritonitis between the two groups (NPGN, 16.2%; all gram positive, 14.2%). Outcomes of peritonitis episodes in the staphylococcal and NPGN groups were analyzed in the presence and absence of STI (Tables 3 and 4). The outcomes in the NPGN peritonitis group were significantly worse (resolution of peritonitis, loss of catheter, hospitalization, and transfer to HD) compared to staphylococcal peritonitis whether a soft tissue infection was present or not. There was no difference in mortality between the groups in the presence or absence of a STI (data not shown).

Episodes of NPGN peritonitis that occurred with a coincidental STI had a significantly lower rate of resolution with up to three courses of antibiotics (NPGN with STI, 36.4% vs. 63.2% without STI, $P = 0.031$), had a higher rate of catheter removal (STI, 63.7% vs. 23.7% without STI, $P < 0.001$), and a higher rate of transferring to hemodialysis (STI, 36.4% vs. 9.6% without STI, $P = 0.003$). There was no difference in the rate of hospitalization or deaths between NPGN peritonitis episodes with or without a coincidental STI. The outcome data for staphylococcal peritonitis episodes with or without a concomitant STI revealed a similar pattern to those in the NPGN group. A significant decrease in resolution (STI, 64% vs. 81.7% without STI, $P = 0.001$), an increase in catheter removal (STI, 30.7% vs. 6.4% without STI, $P < 0.0001$), and an increased transfer to hemodialysis (STI, 16% vs. 1.5% without STI, $P < 0.0001$) was noted in staphylococcal peritonitis episodes that occurred with a STI. There was no difference in hospitalization rates or deaths in the staphylococcal peritonitis group, regardless of the presence or absence of a coincidental STI.

During 1991 there were 106 patients who had a first episode of peritonitis with a single gram positive organism and 32 patients that had a first episode of peritonitis with a single NPGN organism (Table 5). There were no significant demographic differences between the two groups, but there was a trend towards an increase in the subsequent number of peritonitis episodes later in the year in the gram positive group.

Episodes of NPGN peritonitis were treated for significantly longer times with intraperitoneal antibiotics: NPGN episodes were 9.1 ± 8.5 days (mean ± SD) versus 7.1 ± 6.7 days for all gram positive episodes ($P = 0.004$). NPGN peritonitis was also treated for longer periods of time by the oral route: NPGN episodes were 2.7 ± 5.9 days versus 1.7 ± 4.7 days for all gram positive peritonitis ($P = 0.044$). No significant difference in the length of i.v. drug therapy was noted (NPGN 0.6 ± 3.1 day vs. 1.7 ± 6.9 for all gram positive peritonitis, $P = 0.07$).

The 27 reported cases of enterococcal peritonitis were compared to all other forms of gram positive peritonitis and did not differ in such complications or outcomes as incidence of concomitant STI, catheter removal, resolution of peritonitis, or transfer to hemodialysis. There were suggestions of an increase in mortality and hospitalizations in the enterococcal group (death, enterococcus 7.4% vs. other gram positive, 2.2%, $P = 0.087$; hospitalization for enterococcus, 40.7% vs. other gram positive, 24.4%, $P = 0.057$).

When *S. aureus* was compared to all other episodes of gram positive peritonitis, there were significant increases in catheter removal and transfer to hemodialysis (catheter removal for *S. aureus* was 18.12% vs. other gram positive, 6.6%, $P < 0.0001$; transfer to hemodialysis, *S. aureus* 8.7% vs. other gram positive, 1.5%, $P < 0.0001$). There were no significant differences in the

Table 6. Outcomes *S. aureus* vs. coagulase negative staphylococcus

	S. aureus $N = 149$	CNS[a] $N = 242$	*P* value
Resolved	75.8%	83.8%	0.054
Catheter removed	18.1%	4.6%	<0.0001
Hospitalization	29.5%	17.9%	0.007
Transfer to HD	8.7%	1.3%	0.003
Death	3.4%	0.8%	0.068

[a] Coagulase negative staphylococcus

Table 7. Outcomes in the absence of exit site or tunnel infection

	S. aureus $N = 104$	CNS[a] $N = 230$	*P* value
Resolved	82.7%	84.6%	NS
Catheter removed	12.5%	3.1%	.002
Hospitalization	30.1%	17.5%	.015
Transfer to HD	2.9%	0.8%	.18
Death	2.9%	0.8%	.18

[a] Coagulase negative staphylococcus

rate of resolution, hospitalization or death. Thirty percent of the episodes of *S. aureus* peritonitis occurred concomitantly with a STI as compared to 6.0% of the other episodes gram positive peritonitis ($P < 0.0001$).

Compared to all coagulase negative staphylococci (CNS) peritonitis episodes, *S. aureus* peritonitis resulted in a significantly higher rate of catheter removal, hospitalization and transfer to hemodialysis (Table 6). There was a suggestion of a decrease in the rate of resolution of peritonitis and an increase in deaths in the *S. aureus* group. As noted above 30% of the *S. aureus* peritonitis episodes had a concomitant soft tissue infection compared to only 5% for CNS peritonitis ($P < 0.0001$).

To determine if the differences in peritonitis episode outcomes between *S. aureus* and CNS was related to coincidental STIs, we compared the outcomes of peritonitis episodes between these 2 groups in the absence and presence of concomitant STIs (Table 7). Even in the absence of STI, *S. aureus* peritonitis had a significantly higher rate of catheter removal and hospitalization compared to CNS peritonitis. There was no difference in the rate of resolution, transfer to hemodialysis, or death. Even in the presence of a coincidental STI, there were no differences between the *S. aureus* and CNS groups in the following outcome parameters: resolution, catheter removal, hospitalization, transfer to hemodialysis, or death. For some parameters this may simply be a reflection of sample size.

DISCUSSION

The Network 9 Peritonitis and Catheter Survival Study data have been analyzed to examine the differences in the demographics and outcomes in single organism NPGN peritonitis compared to gram positive peritonitis episodes, particularly those caused by *S. aureus* and CNS. The first episode of peritonitis was used for the demographic analysis to minimize the effect of prior peritonitis, a known confounding risk factor [9]. Although the event questionnaires were updated during the course of the infection, the nature of this study is essentially retrospective. This could influence some aspects of severity measures such as frequency of hospitalization and catheter removal. Since the centers had incentives to carefully describe the events, we trust that the data are accurate. While there were no differences in the patient demographics between the NPGN and gram positive peritonitis groups who were experiencing their first episode of peritonitis, the outcomes of the peritonitis episodes was more frequently worse in the NPGN group. Thus, by excluding pseudomonas, polymicrobial contamination, and the role of soft tissue infections, it is clear that gram negative peritonitis results in worse outcomes than peritonitis caused by *S. aureus* or CNS.

Similar to the findings of Tranaeus, Heimburger and Lindholm [11], Network 9 patients with episodes of NPGN and *S. aureus* peritonitis had more severe clinical signs and symptoms than those with other gram positive peritonitis. However, the clinical utility of symptom severity is limited.

There are minimal data that directly compare the outcomes of single organism NPGN peritonitis to that of gram positive peritonitis [16]. The present results show that compared to peritonitis caused by *S. aureus* or CNS, there are significantly worse outcomes with NPGN peritonitis (catheter removal, resolution, hospitalization, transfer to HD) despite longer antibiotic treatment duration by the intraperitoneal and oral routes. Because STIs were coincident to peritonitis, locally defined, and the causative pathogens not recorded, STI data should be cautiously interpreted. Nonetheless, the worse outcomes with NPGN peritonitis could not be attributed to an increased incidence of soft tissue infections. When peritonitis episodes without STI were compared, the outcomes (resolution, catheter removal, hospitalization, and transfer to HD) in the NPGN group were still significantly worse. Episodes of NPGN peritonitis with a coincidental STI had significantly worse resolution rates, higher rates of catheter removal, and change to hemodialysis when compared to gram positive peritonitis with a coincidental STI. Therefore, episodes of NPGN peritonitis have worse outcomes compared to gram positive peritonitis independent of a coincidental soft tissue infection. Enterococcal peritonitis tended to result in an increase of frequency of hospitalization and deaths when compared to other gram positive peritonitis.

In order to examine the outcomes of other gram negative infections, pseudomonal peritonitis was excluded from the present analysis but is described in detail elsewhere [4]. Essentially, episodes of pseudomonal peritonitis were associated with significantly lower rates of resolution (pseudomonas 32.25% vs. 58.8% NPGN, $P < 0.01$) and significantly higher rates of catheter loss (pseudomonas 61.3% vs. 30% other NPGN, $P < 0.002$). There were no significant differences in the rate of transfering to HD (pseudomonas 25.8% vs. 14% for NPGN) or death (pseudomonas 6.5% vs. 3.7% NPGN) between these two groups. The poor outcomes with pseudomonal infections is attributed to the virulence of the organism. The present study expands the comparison of different outcomes by causative pathogen.

The reason for the poor outcomes with NPGN peritonitis is not clear. One possibility is that early in the course of therapy the patients with gram negative peritonitis were not treated with antibiotics to cover gram negative organisms. In a previous Network 9 report, 12 of 73 patients with gram negative organisms on initial gram stain did not initially receive gram negative antibiotic coverage [16]. The Advisory Committee on Peritonitis Management of the International Society of Peritoneal Dialysis recommends to interpret gram stains as preliminary [17, 18], but

did not suggest ignoring the gram stain findings. The outcomes reported here could in part be explained by a delay in the institution of appropriate antibiotic therapy. However, the nature of the data collection does not allow detailed mechanistic hypotheses to be addressed. The transmural migration of bacteria and minute diverticular perforations have been suggested as possible mechanisms in the development of gram negative peritonitis [5, 14]. Touch contamination and catheter related infections are suggested causes for a large portion of gram positive peritonitis episodes [5, 14]. If these are the predominant mechanisms, then the incidence of gram negative peritonitis would be expected to increase in the elderly and possibly in diabetics. In agreement with the data of Holley et al [19], the Network 9 demographic data do not reveal such an increase. Lastly, preliminary experiments in an animal model suggest that *E. coli* peritonitis causes a worse intraperitoneal reaction than does *S. aureus* [20].

Patients with a NPGN peritonitis episode have more severe clinical symptoms and worse outcomes, even in the absence of coincidental STIs, consistent with the observations of Tranaeus et al [11]. This suggests that some other factors inherent to gram negative organisms are responsible. Other possibilities to explain the poor outcomes in the NPGN group include subclinical STIs and the possibility of undiagnosed bowel disease. Significant bowel disease or bowel perforation in peritoneal dialysis patients have been reported to result in a polymicrobial peritonitis [5, 12–14, 21, 22]. Polymicrobial peritonitis was specifically excluded from this analysis to diminish the probability that the source of the bacterium was a bowel leak. Nonetheless, there was a suggestion ($P = 0.06$) of an increase in the incidence of bowel perforations in the NPGN group compared to the gram positive group. Despite the unfavorable outcomes described in this report for NPGN peritonitis and the higher likelihood of bowel disease in the NPGN group, it should be noted that Kiernan et al [12] and Holley et al [13] have suggested that even in polymicrobial peritonitis, an aggressive search for bowel pathology may not always be warranted.

S. aureus peritonitis predisposed patients to catheter removal and transfer to hemodialysis when compared to infection with other gram positive organisms or to CNS. The better outcomes of *S. epidermidis* peritonitis when compared to other forms of peritonitis have been noted before [7–9, 11]. Increased catheter loss was still evident with *S. aureus* peritonitis even in the absence of a STI. However, there were no differences in outcomes in the *S. aureus* and CNS when a soft tissue infection was present. This supports previous observations that a soft tissue infection plays a pivotal role in the outcome of an episode of any type of staphylococcal peritonitis [10, 23, 24].

In the present subset of patients with their first infection, those whose first infection was caused by a gram positive organism were more likely than those whose first infection was caused by a NPGN to have further episodes of peritonitis in 1991. Impaired opsonic activity is related to an increased incidence of gram positive peritonitis [25]. Thus, gram positive peritonitis may be a marker of susceptibility to peritonitis. These Network 9 Study data are consistent with this as well as the observations of Golper and Hartstein [26], who noted that patients with staphylococcal peritonitis were more likely to have subsequent infections by any organisms. Alternatively, patients with NPGN infections are more likely to terminate peritoneal dialysis, thus not having subsequent peritonitis.

The present data suggest that the outcome of non-pseudomonal gram negative peritonitis is significantly worse than the outcome of gram positive peritonitis with or without a concomitant STI. Piraino and her associates [10, 24] have described the dismal prognosis of peritonitis complicated by a coincidental STI. The present data extend this concern in that a soft tissue infection is associated with a lower rate of resolution, a higher rate of catheter removal, and a higher rate of transfer to hemodialysis in both the non-pseudomonal gram negative and gram positive groups.

Peritonitis caused by a single non-pseudomonal gram negative organism appears to be a more serious infection than was previously thought. While with NPGN infections there was a statistically significant increase in the frequency of fever, nausea/vomiting, and abdominal pain, this observation may not be clinically useful. NPGN infections led to more prolonged antibiotics and worse outcomes. Undetected bowel leaks or STIs may have been present. This warrants further study. In addition, the poor outcomes even with more protracted antibiotic therapy raises a concern as to the appropriate duration and intensity of management of these infections. This concern may be raised specifically regarding the practice within Network 9 (discussed in [13]) or for formal recommendations. The Advisory Committee on Peritonitis Management of the International Society of Peritoneal Dialysis recommends a 14-day antibiotic course for NPGN (referred to as non-Xanthomonas) peritonitis and a 21-day course for *S. aureus* peritonitis [17]. While a longer duration of antibiotic therapy may not improve outcomes, it seems reasonable to reassess the NPGN recommendation in light of the present findings.

These data lend strong support to the notion that the natural history of apparently appropriately treated peritonitis differs by the type of causative pathogen. All peritonitis episodes are not equivalent in terms of outcomes. In light of the clearly different outcomes of peritonitis caused by different pathogens, the information transmitted by an infection rate is of limited value. The concept of the "peritonitis infection rate" must be used selectively and cautiously for certain comparisons. For example, from the data presented in this report, a single episode of NPGN peritonitis may lead to more prolonged illness than an episode of *S. epidermidis* peritonitis, and this may affect nutritional parameters differently. Yet only one episode occurred in each case and assuming equal time at risk, the "rate" was the same. One episode of GNPN peritonitis will more likely lead to termination of peritoneal dialysis than an episode caused by a gram positive pathogen. The influence of "peritonitis rate," rather than causative pathogen, on mortality is especially suspect [27]. Thus, the concept of "peritonitis rate" is only meaningful when specific organisms are considered. Additional variables, such as duration of cloudy fluid, anorexia, and transport abnormalities, etc., must somehow be utilized to compare the ultimate consequences of peritonitis. The peritoneal dialysis community needs to address this issue, particularly in the present regulatory and competitive (and thus comparative) environment.

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REFERENCES

1. LINDBLAD AS, NOVAK JW, NOLPH KD: *Continuous Ambulatory Peritoneal Dialysis in the USA: Final Report of the National CAPD Registry.* Dordrecht, Kluwer Academic Publishers, 1989
2. MAIORCA R, VONESH EF, CAVALLI PL, DE VECCHI A, GIANGRANDE A, LA GRECA G, SCARPIONI LL, BRAGANITINI L, CANCARINI GC, CANTALUPPI A, CASTELINOVO C, CASTIGLIONI A, POISETTI PG, VIGLINO G: A multicenter, selection-adjusted comparison of patient and technique survivals on CAPD and haemodialysis. *Perit Dial Int* 11:118–127, 1991
3. GOLPER TA, GEERLINGS W, SELWOOD NH, BRUNNER FP, WING AJ: Peritoneal dialysis results in the EDTA Registry, in *Peritoneal Dialysis* (3rd ed), edited by NOLPH E, Dordrecht, Kluwer Academic Publishers, 1989, pp 414–428
4. BUNKE CM, BRIER ME, GOLPER TA: Pseudomonas peritonitis in peritoneal dialysis patients: The Network 9 peritonitis study. *Am J Kid Dis* 25:769–774, 1995
5. PIRAINO BM: Infections in peritoneal dialysis, in *Clinical Dialysis* (3rd ed), edited by NISSENSON AR, FINE RN, GENTILE DE, Norwalk, Appleton & Lange, 1995, pp 426–449
6. NAGAPPAN R, COLLINS JF, LEE WT: Fungal peritonitis in continuous ambulatory peritoneal dialysis: The Auckland experience. *Am J Kid Dis* 20:492–496, 1992
7. FOX L, TZAMALOUKAS AH, MURATA GH: Metabolic differences between persistent and routine peritonitis in continuous ambulatory peritoneal dialysis (CAPD). *Adv Perit Dial* 8:346–350, 1992
8. VAS SI: Etiology and treatment of peritonitis. *Trans Am Soc Artif Intern Organs* 30:682–684, 1984
9. GOLPER TA, BRIER, ME, BUNKE CM, SCHREIBER MJ, BARTLETT DK, HAMILTON RW, STRIFE F, HAMBURGER RJ: Risk factors for peritonitis in chronic peritoneal dialysis: The network 9 peritonitis and catheter survival studies. *Am J Kid Dis* 28:428–436, 1996
10. GUPTA B, BERNARDINI J, PIRAINO B: Peritonitis associated with exit site and tunnel infections. *Am J Kid Dis* 28:415–419, 1996
11. TRANAEUS A, HEIMBURGER O, LINDHOLM B: Peritonitis in continuous ambulatory peritoneal dialysis (CAPD): Diagnostic findings, therapeutic outcome and complications. *Perit Dial Int* 9:179–190, 1989
12. KIERNAN L, FINKELSTEIN FO, KLIGER AS, GORBAN-BRENNAN N, JUERGENSEN P, MOORAKI A, BROWN E: Outcome of polymicrobial peritonitis in continuous ambulatory peritoneal dialysis patients. *Am J Kid Dis* 25:461–464, 1995
13. HOLLEY JL, BERNARDINI J, PIRAINO B: Polymicrobial peritonitis in patients on continuous peritoneal dialysis. *Am J Kid Dis* 19:162–166, 1992
14. VAS SI: Peritonitis, in *Peritoneal Dialysis* (3rd ed), edited by NOLPH KD, Boston, Kluwer Academic Publishers, 1989, pp 261–288
15. BUNKE M, BRIER ME, GOLPER TA: Culture negative CAPD peritonitis: The Network 9 Study. *Adv Perit Dial* 10:174–178, 1994
16. BRIER ME, ARONOFF GR: Initial intraperitoneal therapy for CAPD peritonitis: The Network 9 peritonitis study. *Adv Perit Dial* 10:141–143, 1994
17. KEANE WF, ALEXANDER SR, BAILIE GR, BOESCHOTEN E, GOKAL R, GOLPER TA, HOLMES CJ, HUANG C-C, KAWAGUCHI Y, PIRAINO B, RIELLA M, SCHAEFER F, VAS S: Peritoneal dialysis related peritonitis treatment recommendations, 1996 update: The Ad Hoc Advisory Committee on Peritonitis Management. *Perit Dial Int* 16:557–573, 1996
18. KRAUS ES, SPECTOR DA: PD peritonitis: Course dependence on bacterial species, in *Advances in Peritoneal Dialysis*; Proceedings of the Second International Symposium on Peritoneal Dialysis, Berlin, June 16–19, 1981 (International Congress Series No. 567), Amsterdam, Excerpta Medica, 1981, pp 302–304
19. HOLLEY JL, BERNARDINI J, PERLMUTTER JA, PIRAINO B: A comparison of infection rates among older and younger patients on continuous peritoneal dialysis. *Perit Dial Int* 14:66–69, 1994
20. PAWLACZYK K, KUZIAN M, WIECZOROWSKA-TOBIS K, POLUBINSKA A, MIRSKA I, BREBOROWICZ A, OREOPOULOS DG: An animal model for acute peritonitis. Various microbes produce different responses. (abstract) *Perit Dial Int* 17(suppl 1):S36, 1997
21. TZAMALOUKAS AH, OBERMILLER LE, GIBEL LJ, MURATA GH, WOOD B, SIMON D, ERICKSON DG, KANIG SP: Peritonitis associated with intra-abdominal pathology in continuous ambulatory peritoneal dialysis patients. *Perit Dial Int* 13:S335–S337, 1993
22. WAKEEN MJ, ZIMMERMAN SW, BIDWELL D: Viscus perforation in peritoneal dialysis patients: Diagnosis and outcome. *Perit Dial Int* 14:371–377, 1994
23. ZIMMERMAN SW, O'BRIEN M, WIEDENHOEFT FA, JOHNSON CA: *Staphylococcus aureus* peritoneal catheter-related infections: A cause of catheter loss and peritonitis. *Perit Dial Int* 8:191–194, 1988
24. PIRAINO B: Management of catheter-related infections. *Am J Kid Dis* 27:754–758, 1996
25. KEANE WF, COMTY CM, VERBRUGH HA, PETERSON PK: Opsonic deficiency of peritoneal dialysis effluent in continuous ambulatory peritoneal dialysis. *Kidney Int* 25:539–543, 1984
26. GOLPER TA, HARTSTEIN AI: Analysis of the causative pathogens in uncomplicated CAPD-associated peritonitis: Duration of therapy, relapses, and prognosis. *Am J Kid Dis* 7:141–145, 1986
27. FRIED LF, BERNARDINI J, JOHNSTON JR, PIRAINO B: Peritonitis influences mortality in peritoneal dialysis patients. *J Am Soc Nephrol* 7:2176–2182, 1996